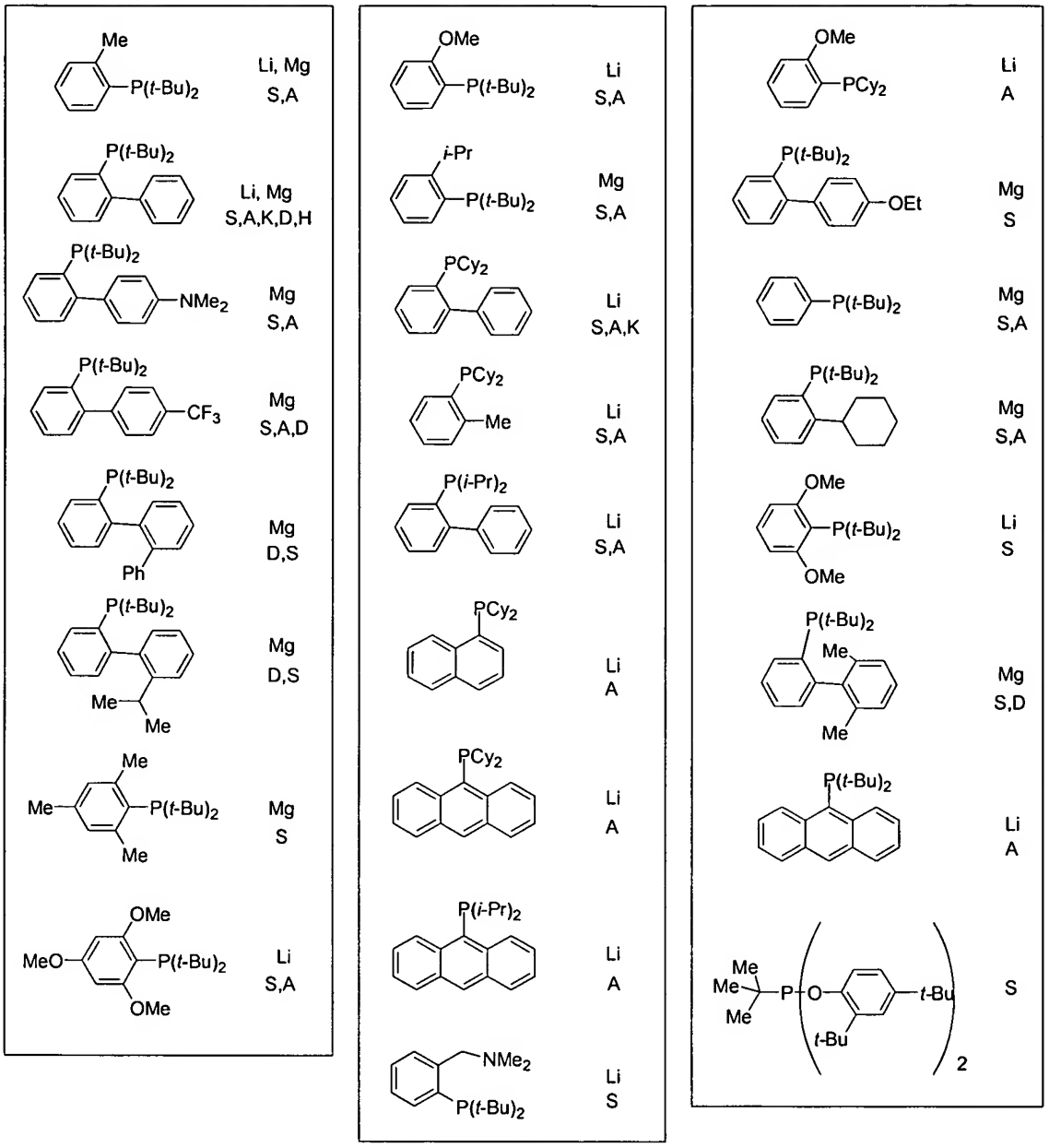
Figure 1. Method of Preparation and Reactions Screened for Various Ligands.

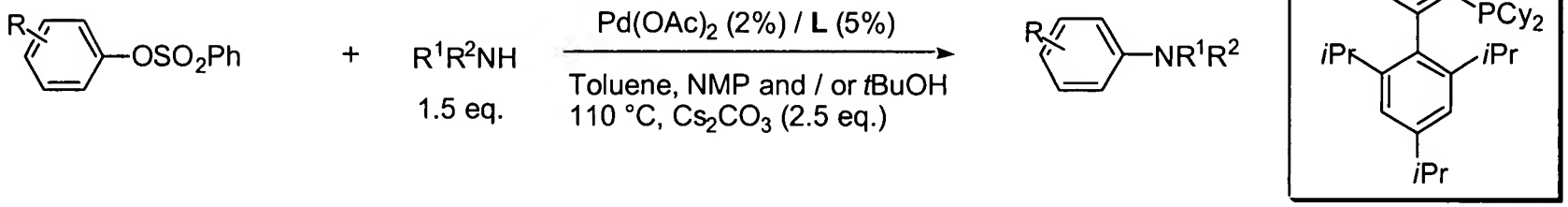


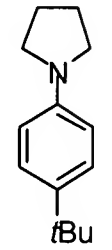
Legend

Method of Preparation:
Li= made from organolithium reagent
Mg= made from Grignard reagent

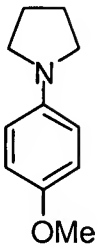
Reactions Screened:
S=Used for Suzuki Coupling
A=Used for amination
D=Used for diaryl ether synthesis
K=Used for ketone arylation
H=Used for Heck reaction

Pd-Catalyzed C-N Bond Formation on Benzenesulfonates

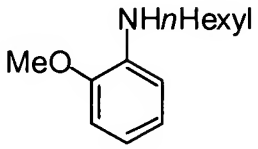




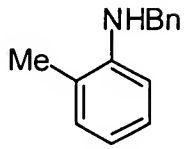
98% yield



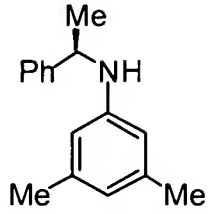
87% yield
8% **L** was used



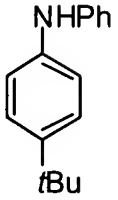
87% yield



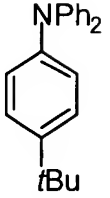
88% yield



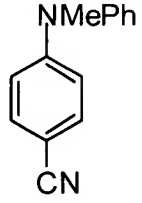
92% yield, rxn temp. was 90 °C
ee of starting material: 96%
ee of product: 94%



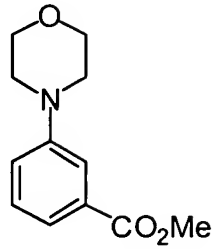
95% yield



92% yield

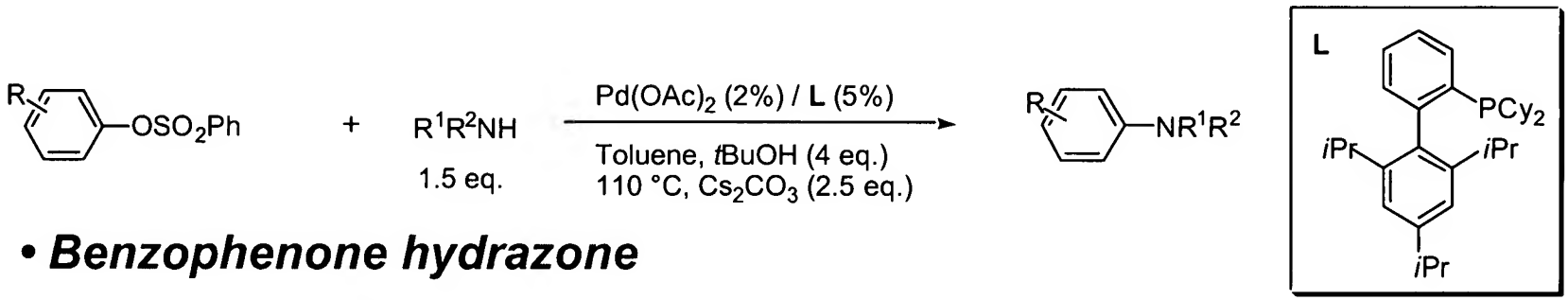


91% yield
From tosylate,
K_3PO_4 was the base

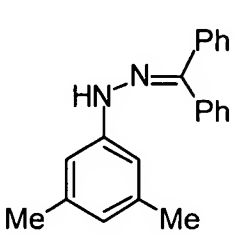


> 99% yield
From tosylate

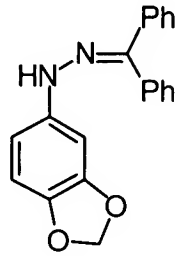
Pd-Catalyzed C-N Bond Formation on Benzenesulfonates



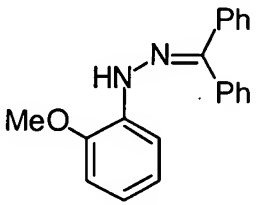
• Benzophenone hydrazone



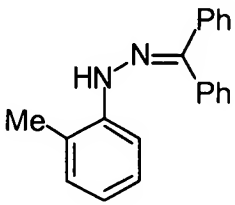
99% yield



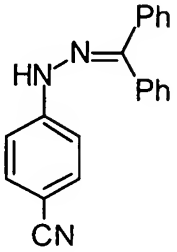
99% yield



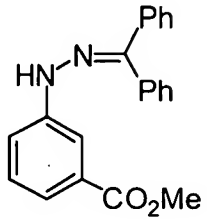
97% yield



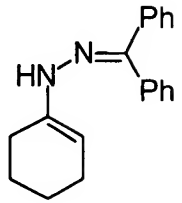
90% yield



94% yield
From tosylate,
K_3PO_4 was the base

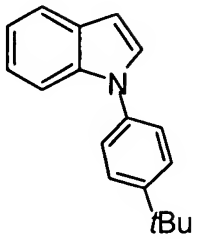


86% yield
From tosylate

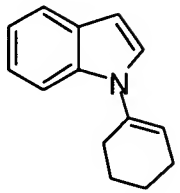


58% yield
From tosylate

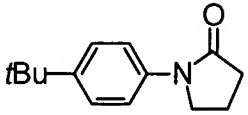
• Indole and amide*



> 99% yield
K_3PO_4 was the base

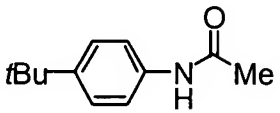


100% GC yield
K_3PO_4 was the base



95% yield

K_2CO_3 was the base,
*t*BuOH was the solvent.



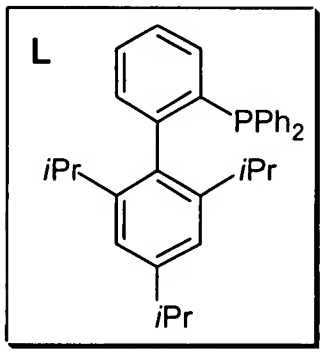
88% yield

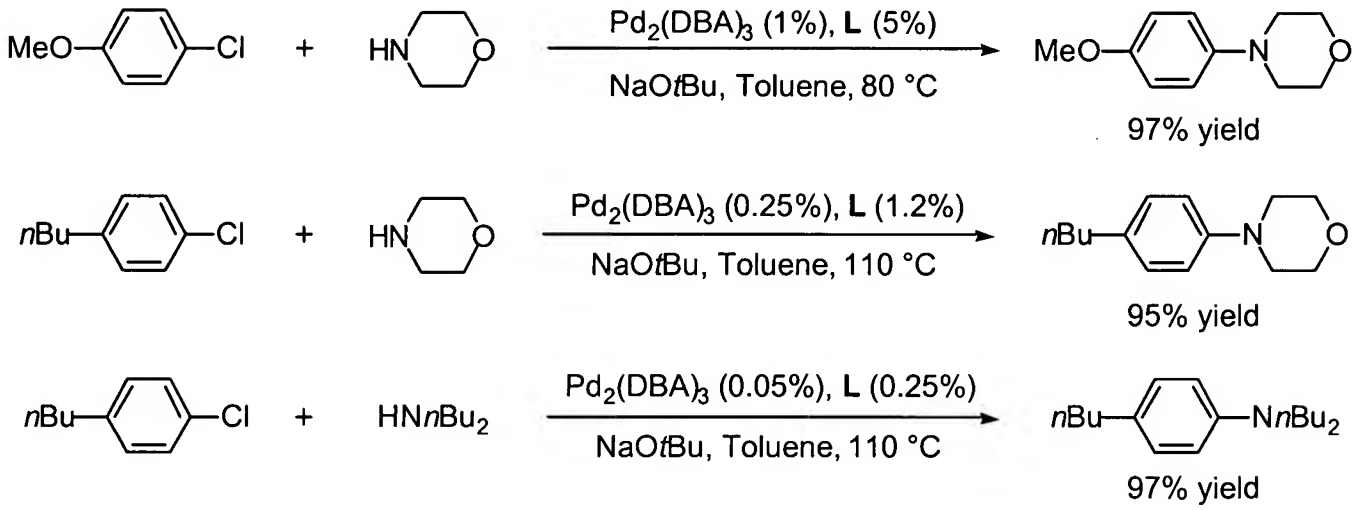
K_2CO_3 was the base,
*t*BuOH was the solvent.

* $Pd(OAc)_2$ was pre-reduced with $PhB(OH)_2$ (5%) in the presence of ligand.

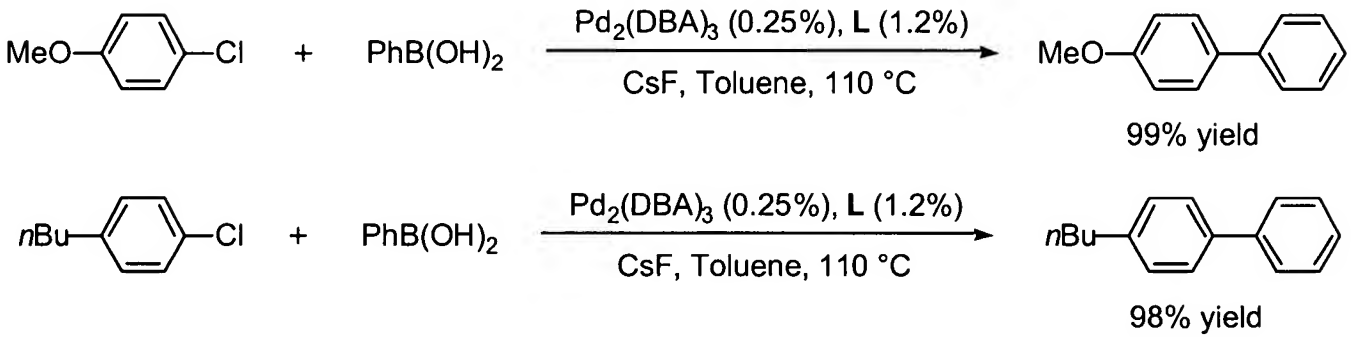
Pd /Ar_3P on Aryl Chlorides in Cross Coupling Reactions

Amination



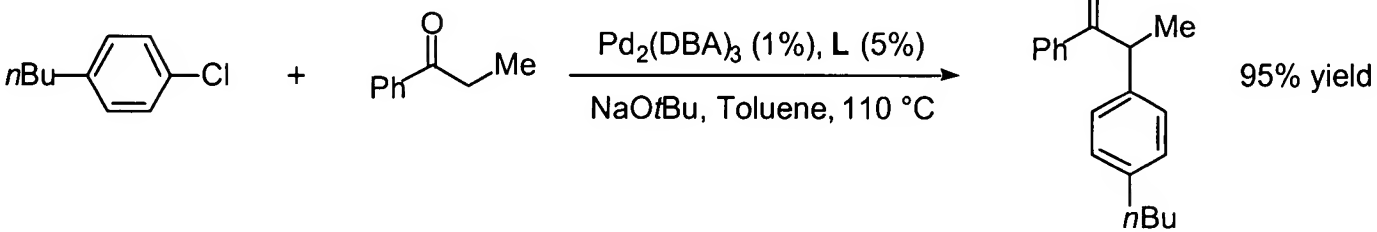


Suzuki reaction

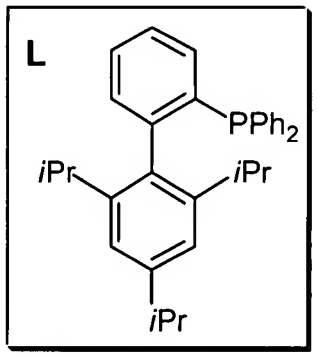


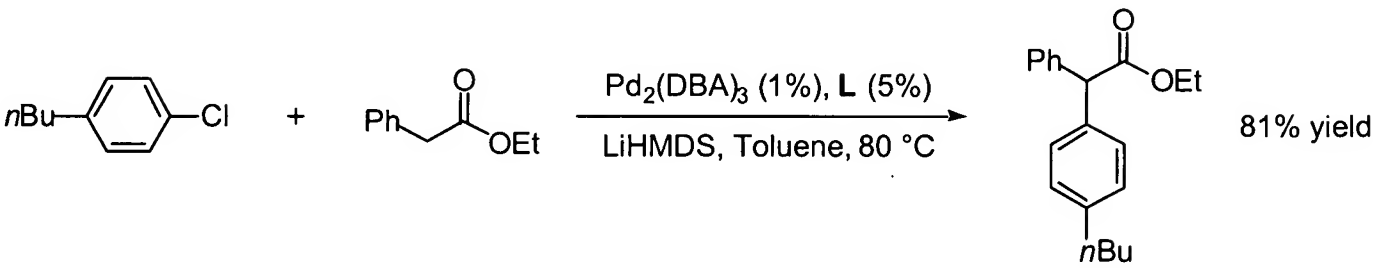
Pd /Ar_3P on Aryl Chlorides in Cross Coupling Reactions

- ***Arylation on ketone and esters***

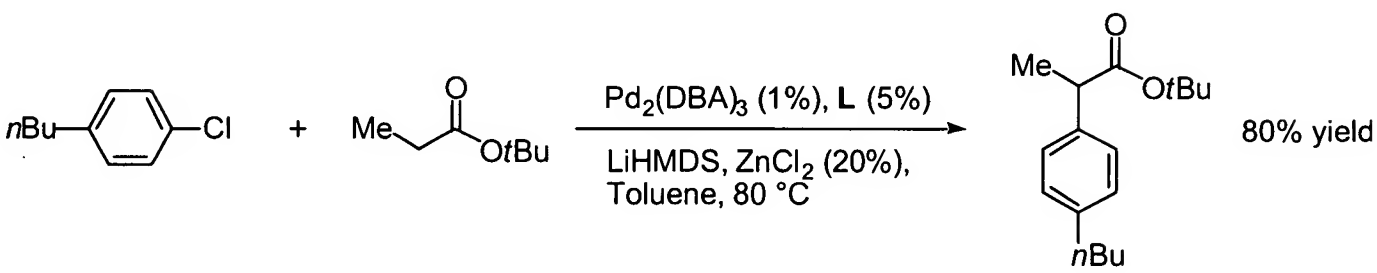


95% yield



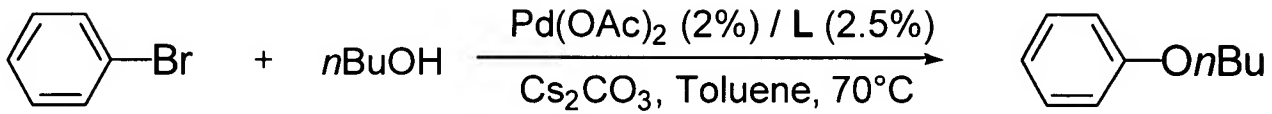


81% yield



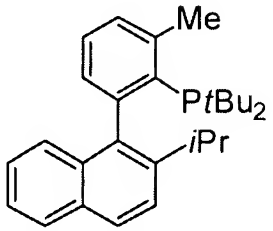
80% yield

Ligand Comparison

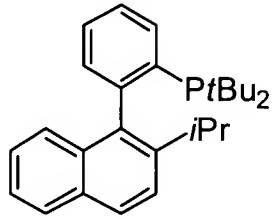


•The presence of a substituent in the 6-position of the phosphine-containing ring is beneficial.

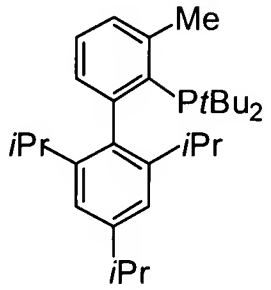
L



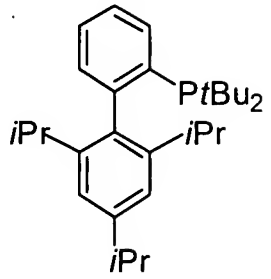
GC yield of desired product: 97%



44%



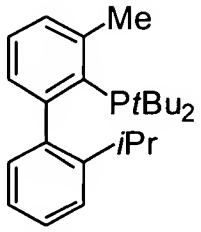
80%



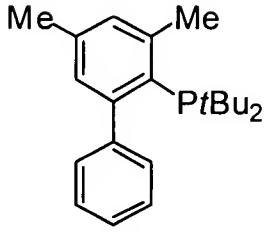
26%

-207-

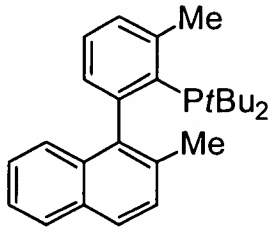
L



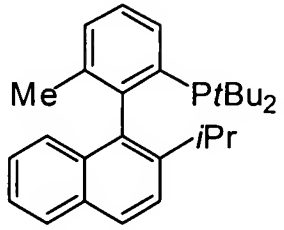
GC yield of desired product: 29%



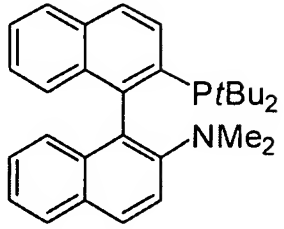
3%



65%

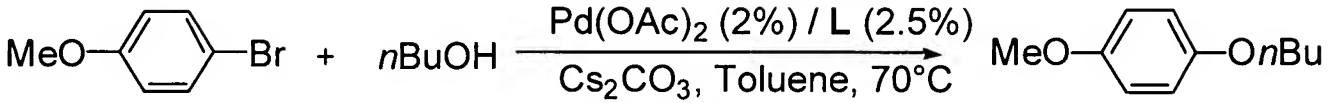


85%

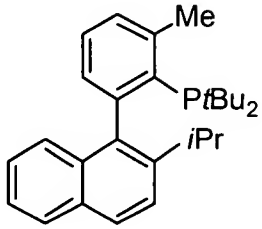


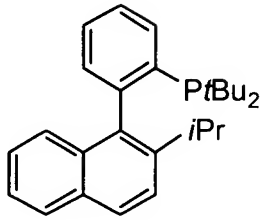
66%

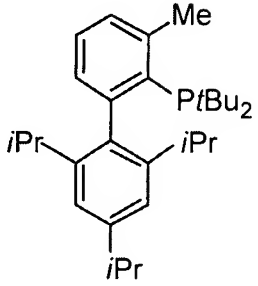
Ligand Comparison

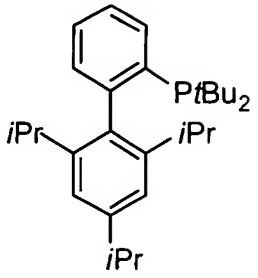


L



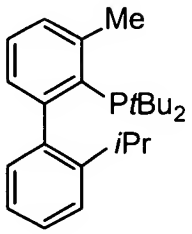


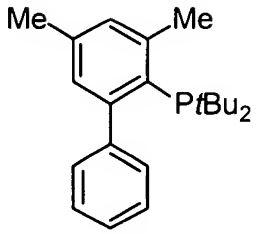


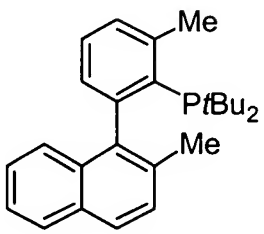


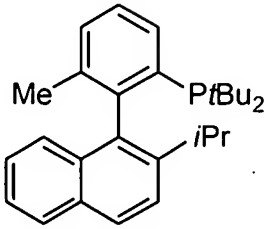
GC yield of desired product: 28% | 8% | 77% | 3%

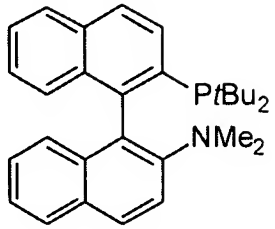
L





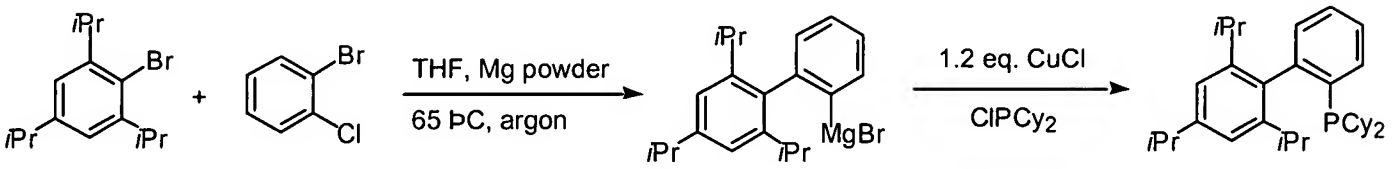






GC yield of desired product: 19% | 1% | 20% | 36% | 12%

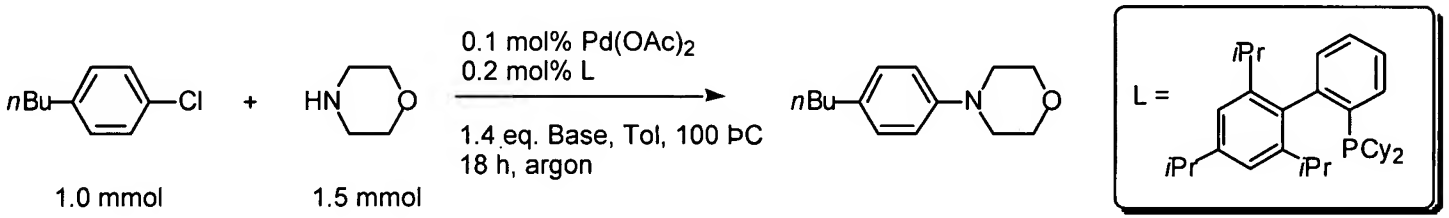
Preparation of biaryl phosphine ligand



20 mmol 20 mmol 55% isolated yield

Pd-catalyzed Amination of Aryl Chloride: Base Effect

0.1 mol% Pd, 100 ÞC



1.0 mmol 1.5 mmol

entry	base	% conv. of ArCl	% GC yield[a]
1	K_3PO_4	1	0
2	$K_3PO_4 \cdot H_2O$	2	0
3	K_2CO_3	2	0
4	Cs_2CO_3	8	3
5	NaO*t*Bu	98	87[b]
6	KOAc	2	0
7	KOH	100	98 (98% iso. yield)

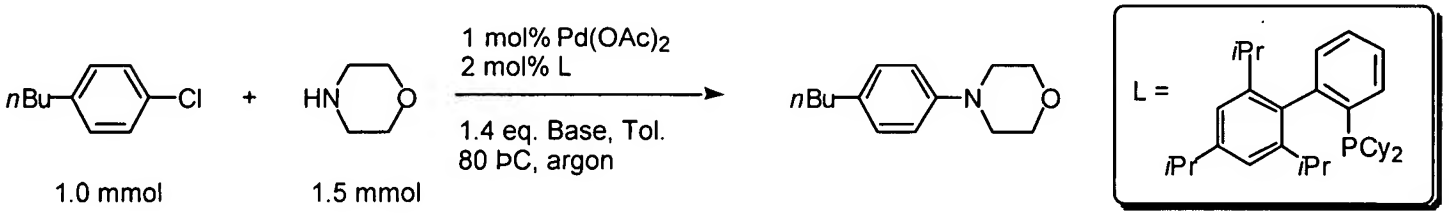
[a] Dodecane was used as the internal standard.

[b] 2% reduction product was observed.

1-210-1

Pd-catalyzed Amination of Aryl Chloride: Base Effect

1 mol% Pd, 80 ÞC

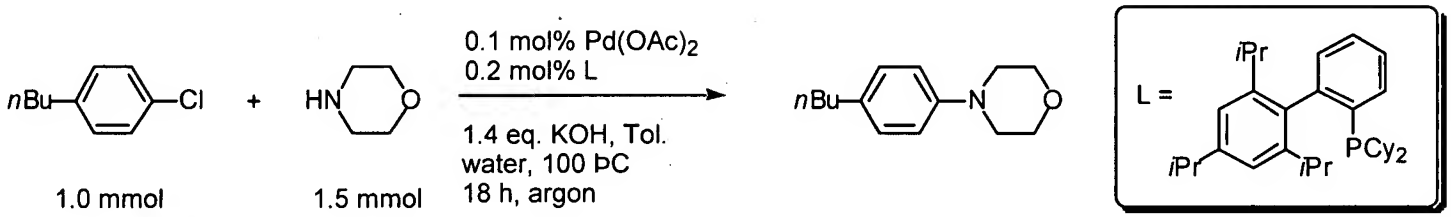


1.0 mmol 1.5 mmol

entry	base	2 hours % conv. of ArCl	2 hours % GC yield[a]	18 hours % conv. of ArCl	18 hours % GC yield[a]
1	K_3PO_4	11	11	65	63
2	$K_3PO_4 \cdot H_2O$	23	23	72	69
3	K_2CO_3	1	1	39	38
4	Cs_2CO_3	18	18	97	93
5	NaO*t*-Bu	>99	>99	/	/
6	KOH	99	99	/	/
7	NaOH	72	72	>99	96

[a] Dodecane was used as the internal standard.

Pd-catalyzed Amination of Aryl Chloride: Water Effect

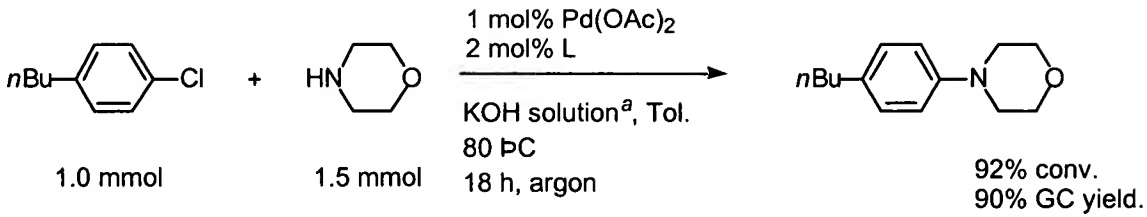


1.0 mmol 1.5 mmol

entry	mol% of water (vol)	% conv. of ArCl	% GC yield[a]
1	0 (0 µL)[b]	100	>99
2	50 (9 µL)[b]	92	88
3	100 (18 µL)[b]	100	98
4	200 (36 µL)[b]	78	74
5	500 (90 µL)[c]	1	1

[a] Dodecane was used as the internal standard.
[b] KOH suspension was observed.
[c] Clear solution was observed.

aq. KOH solution:

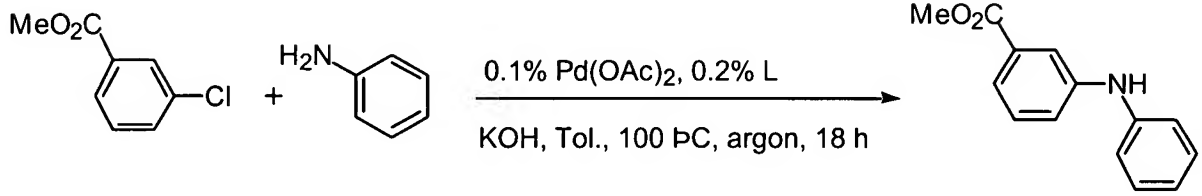


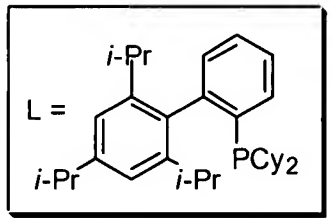
1.0 mmol 1.5 mmol

92% conv.
90% GC yield.

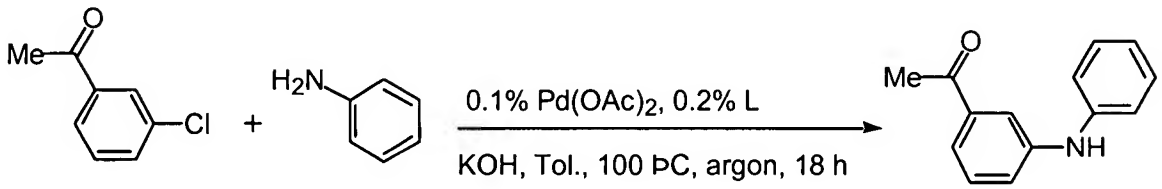
[a] 0.1 mL of 14 M KOH solution was added.

Preliminary Substrate scope using KOH base with 0.1% Pd



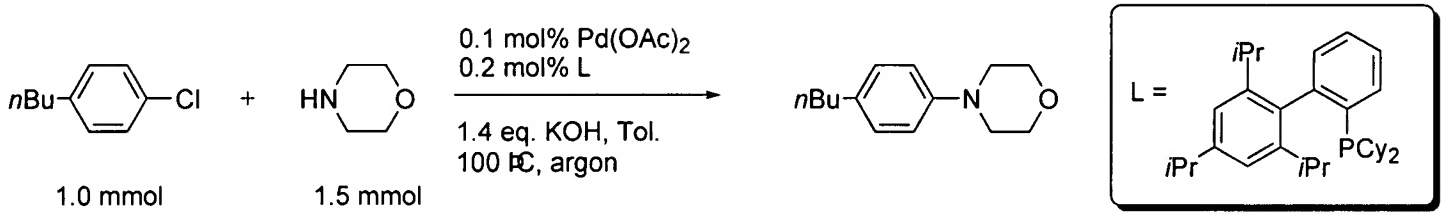


Entry	Additon of water	% Conv.	%GC yield
1	0	100	18
2	1 eq. (18µL)	100	76 (iso)



Entry	Additon of water	% Conv.	% uncorrected GC yield
1	0	100	73 (88 iso.)
2	1 eq. (18µL)	100	73

Pd-catalyzed Amination of Aryl Chloride: Reaction Time

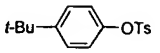
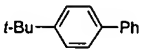


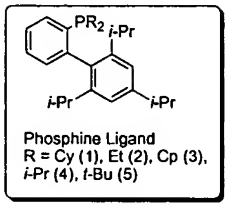
1.0 mmol 1.5 mmol

entry	Time/ h	% GC yield[a]
1	1	23
2	2	48
3	3	78
4	5	>99

[a] Dodecane was used as the internal standard.

Figure 14

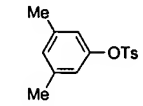
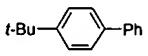
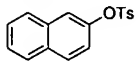
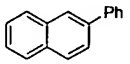
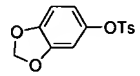
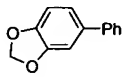
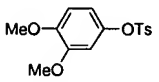
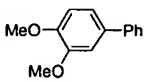
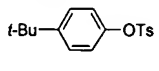
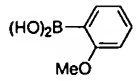
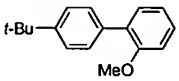
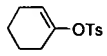
Entry	Aryl Tosylate	Boronic Acid	Pd/L (mol%)[a]	Base (3 equiv)	Solvent	Temperature (°C)	Time (h)	Product	% Yield
1		$PhB(OH)_2$	2/5	$K_3PO_4 \cdot H_2O$	THF	80	3		94
			2/5	$K_3PO_4 \cdot H_2O$	Dioxane	90	5		100 (GC)
			2/5	K_3PO_4	Dioxane	130	22		92
			1/2	CsF	THF	90	19		98
			2/5	KF	THF	90	18		4 (GC)
			2/5	Cs_2CO_3	THF	90	18		65 (GC)
			2/5	K_3PO_4	THF	90	5		93 (GC)
			2/5	KF	Dioxane	90	16		63 (GC)
			2/5	CsF	Dioxane	90	16		86 (GC)
			2/5	Cs_2CO_3	Dioxane	90	16		96 (GC)
			2/5	K_3PO_4	Dioxane	90	5		94 (GC)
			2/5	KF	Toluene	90	16		61 (GC)
			2/5	CsF	Toluene	90	23		57 (GC)
			2/5	Cs_2CO_3	Toluene	90	23		61 (GC)
			2/5	K_3PO_4	Toluene	90	5		93 (GC)
			2/5	K_3PO_4	DME	90	24		87(GC)
			2/5[b]	$K_3PO_4 \cdot H_2O$	THF	80	23		72 (GC)
			2/5[c]	$K_3PO_4 \cdot H_2O$	THF	80	23		98(GC)
			2/5[d]	$K_3PO_4 \cdot H_2O$	THF	80	23		82(GC)



Phosphine Ligand
R = Cy (1), Et (2), Cp (3), *i*-Pr (4), *t*-Bu (5)

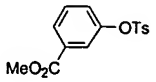
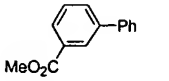
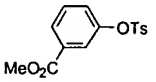
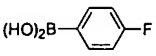
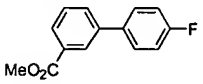
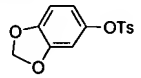
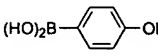
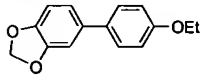
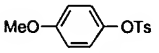
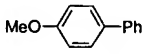
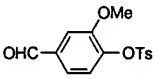
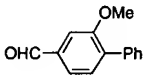
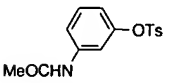
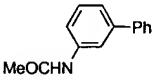
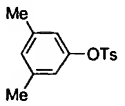
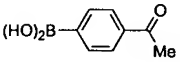
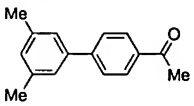
[a] $Pd(OAc)_2$ and the phosphine ligand 1 (R = Cy) were used. [b] Phosphine ligand 2 (R = Et). [c] Phosphine ligand 3 (R = Cp).
[d] Phosphine ligand 5 (R = *t*-Bu).

Figure 15

Entry	Aryl Tosylate	Boronic Acid	Pd/L (mol%)[a]	Base (3 equiv)	Solvent	Temperature (°C)	Time (h)	Product	% Yield
1		$PhB(OH)_2$	2/5 2/5 1/2	$K_3PO_4 \cdot H_2O$ K_3PO_4 CsF	THF Dioxane THF	80 130 90	3 23 19		92 95 89
2		$PhB(OH)_2$	2/5 1/2	K_3PO_4 CsF	Dioxane THF	130 90	23 19		91 98
3		$PhB(OH)_2$	2/5 2/5	K_3PO_4 $K_3PO_4 \cdot H_2O$	Dioxane THF	130 80	24 3		91 91
4		$PhB(OH)_2$	2/5	K_3PO_4	Dioxane	130	24		68
5			2/5	K_3PO_4	Dioxane	130	19		92
6		$PhB(OH)_2$	1/2	K_3PO_4	Dioxane	90	19		78

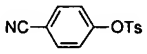
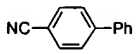
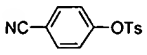
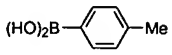
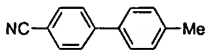
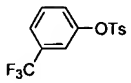
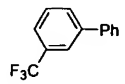
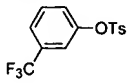
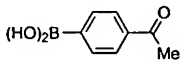
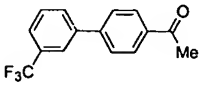
[a] $Pd(OAc)_2$ and the phosphine ligand 1 (R = Cy) were used.

Figure 16

Entry	Aryl Tosylate	Boronic Acid	Pd/L (mol%)[a]	Base (3 equiv)	Solvent	Temperature (°C)	Time (h)	Product	% Yield
1		$PhB(OH)_2$	1/2 2/5	CsF K_3PO_4	THF Dioxane	90 130	19 19		91 95
2			1/2 2/5	$K_3PO_4 \cdot H_2O$ $K_3PO_4 \cdot H_2O$	THF THF	90 90	7 7		87 95
3			1/2 2/5	CsF K_3PO_4	THF Dioxane	90 130	14 22		95 95
4		$PhB(OH)_2$	2/5	K_3PO_4	Dioxane	130	22		93
5		$PhB(OH)_2$	1/2	$K_3PO_4 \cdot H_2O$	THF	90	4		90
6		$PhB(OH)_2$	1/2	CsF	THF	90	24		64
7			2/5	$K_3PO_4 \cdot H_2O$	THF	90	6		86

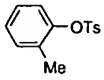
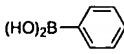
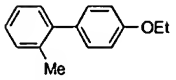
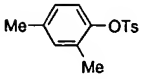
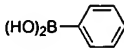
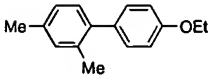
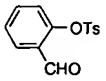
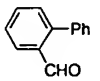
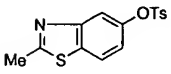
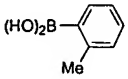
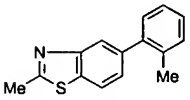
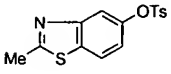
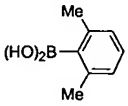
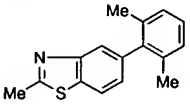
[a] $Pd(OAc)_2$ and the phosphine ligand 1 (R = Cy) were used.

Figure 17

Entry	Aryl Tosylate	Boronic Acid	Pd/L (mol%)[a]	Base (3 equiv)	Solvent	Temperature (°C)	Time (h)	Product	% Yield
1		$PhB(OH)_2$	2/5	K_3PO_4	Dioxane	130	19		64
2			2/5 5/10	$K_3PO_4 \cdot H_2O$ $K_3PO_4 \cdot H_2O$	THF THF	90 90	3 3		72[b] 76[c]
3		$PhB(OH)_2$	1/2	CsF	THF	90	19		31[d]
4			2/5	$K_3PO_4 \cdot H_2O$	THF	90	3		62[e]

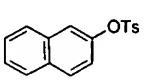
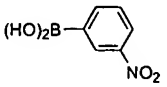
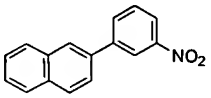
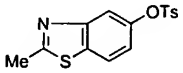
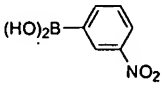
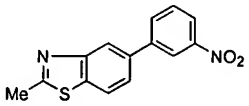
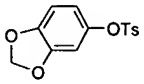
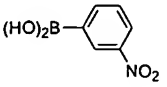
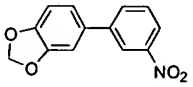
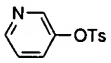
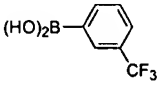
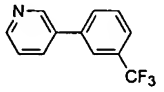
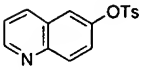
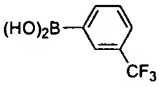
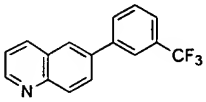
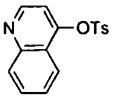
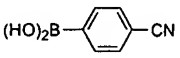
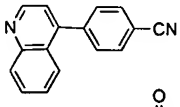
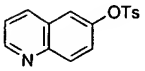
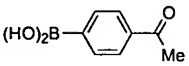
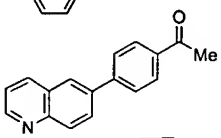
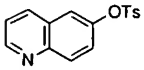
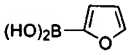
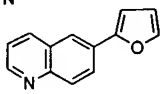
[a] $Pd(OAc)_2$ and the phosphine ligand 1 (R = Cy) were used. [b] 28% of 4-cyanophenol was also isolated. [c] 20% of 4-cyanophenol was also isolated. [d] 10% of 4-cyanophenol was also isolated. [e] 22% of 3-(α,α,α-trifluromethyl)phenol was also isolated

Figure 18

Entry	Aryl Tosylate	Boronic Acid	Pd/L (mol%)[a]	Base (3 equiv)	Solvent	Temperature (°C)	Time (h)	Product	% Yield
1		$PhB(OH)_2$	1/2	CsF	THF	90	19		93
2		$(HO)_2B$— 	1/2	$K_3PO_4 \cdot H_2O$	THF	90	23		73
3		$(HO)_2B$— 	2/5	$K_3PO_4 \cdot H_2O$	Dioxane	110	23		86
			2/5	$K_3PO_4 \cdot H_2O$	Dioxane	100	23		58 (GC)
			2/5[b]	$K_3PO_4 \cdot H_2O$	Dioxane	100	23		64 (GC)
			2/5[b]	$K_3PO_4 \cdot H_2O$	Dioxane	110	23		94 (GC)
4		$PhB(OH)_2$	1/2	$K_3PO_4 \cdot H_2O$	THF	90	23		89
5			2/5	$K_3PO_4 \cdot H_2O$	THF	80	3		97
6			2/5	$K_3PO_4 \cdot H_2O$	Dioxane	110	13		85
			2/5[b]	$K_3PO_4 \cdot H_2O$	Dioxane	110	23		97 (GC)

[a] $Pd(OAc)_2$ and the phosphine ligand 1 (R = Cy) were used. [b] Phosphine ligand 4 (R = *i*-Pr).

Figure 19

Entry	Aryl Tosylate	Boronic Acid	Time (h)	Product	Isolated Yield (%)
1			3		94
2			3		91
3			5		81
4			3		94
5			3		91
6			5 3		83 78
7			3		91
8			3		39

Conditions: Aryl tosylate (1 equiv), arylboronic acid (2 equiv), $Pd(OAc)_2$ (2%), Phosphine ligand 1 (5%), $K_3PO_4 \bullet H_2O$ (3 equiv), THF, 80 °C.